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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/978,375	10/16/2001	Avi J. Ashkenazi	GNE.2630P1C24	4717

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HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 01/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,375	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/1/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 11/1/2005. The amendment filed 11/1/2005 is acknowledged. The amendment has been entered. Claims 58-70 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 11/1/2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 58-62, 69 and 70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to isolated polypeptides wherein the polypeptides have at least 80%, 85%, 90%, 95% or 99% sequence identity with the sequence disclosed as SEQ ID NO: 59 (PRO363) wherein the polypeptide induces chondrocyte re-differentiation. The claims do not require that the nucleic acids possess any particular conserved structure, or other disclosed distinguishing structural feature.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity and the functional characteristic that the sequence encodes a polypeptide which can induce chondrocyte redifferentiation. There is not even an identification of any particular portion of the structure that must be conserved or that is required for the indicated function. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics including lack of a structure/function relationship, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 58-70 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2002/0055139 A1 (HOLTZMAN et al., published May 9, 2002 with priority to 09/312,359, filed May 14, 1999).

HOLTZMAN teaches a polypeptide (human A236 protein) that is 100% identical to SEQ ID NO: 59 (See attached sequence alignment), (e.g., see HOLTZMAN paragraph [0129] describing Figure 23, SEQ ID NO: 23 and SEQ ID NO: 24). Since the polypeptide taught by HOLTZMAN is 100% identical to SEQ ID NO: 59, it would necessarily encode the extracellular domain of SEQ ID NO: 59. HOLTZMAN also teaches the mature form of the A236 protein and indicates that the mature form results from cleavage of the signal peptide (e.g., see paragraphs [0302], [0303] and [0314]). Therefore, the mature form of the A236 protein lacks its associated signal peptide, and the mature form of the A236 protein would necessarily be a polypeptide comprising the extracellular domain of SEQ ID NO: 59 lacking its associated signal peptide. HOLTZMAN also teaches that the A236 protein can be a chimeric polypeptide comprising a polypeptide fused to a heterologous polypeptide (e.g., see paragraph [0595]). Specifically, HOLTZMAN teaches that the chimeric polypeptide comprises a GST sequence (i.e., an epitope tag) (e.g., see paragraph 0597]) or an immunoglobulin constant region (i.e., an Fc region of an immunoglobulin).

Response to Arguments

Applicant's arguments filed 11/1/2005 have been fully considered.

With respect to the rejection of claims under 35 USC 112, 1st paragraph (Written Description) Applicants arguments have been fully considered. With respect to the limitations "signal peptide", "extracellular domain" and "extracellular domain lacking its associated signal

peptide" it is acknowledged that the specification has provided adequate description for these specific limitations.

With respect to Applicants arguments that the specification has provided a detailed description of the chondrocyte redifferentiation assay (Example 126) and that one of skill in the art would be able to use the assay to identify which of the claimed sequences can induce chondrocyte redifferentiation, the arguments are not persuasive. Applicants assert that Example 126 of the instant application provide detailed protocols for the chondrocyte redifferentiation assay. Applicants contend that by following the instant disclosure, one of skill in the art can easily test whether a claimed variant of the PRO363 polypeptide induces chondrocyte redifferentiation. Applicants also argue that methods for determining percent identity between two sequences is disclosed in the specification, as well as guidance to make changes to PRO polypeptide sequences without adversely affecting its activity. Applicant urges that such provides basis for the newly claimed genus of sequences with at least 80-99% sequence identity to SEQ ID NO: 59 and *which are functionally defined as being able to induce chondrocyte redifferentiation*. Applicant points to the specification's disclosure of methods for the determination of percent identity, and assays for identification of polypeptides and for support of the functional limitation in the claims. Applicants urge that the skilled artisan can readily test sequences for identity and whether or not the encoded polypeptides can induce chondrocyte redifferentiation. Therefore, Applicants contend that one of skill in the art would be able to identify and make the claimed sequences.

Applicants' arguments have been fully considered, but are not persuasive. The courts have specifically stated that the skilled artisan cannot envision the *detailed chemical structure* of

an encompassed polypeptide until the structure is disclosed, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In the instant case only SEQ ID NO: 59 (PRO363) has been disclosed as being able to induce chondrocyte redifferentiation. However, the specification does not disclose any variants of the PRO363 polypeptide (SEQ ID NO: 59) which can induce chondrocyte redifferentiation. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factors present in the claims are a partial structure in the form of a recitation of percent identity, and a requirement that the polypeptide can induce chondrocyte redifferentiation. ***There is no identification of any particular portion of the structure that must be conserved in order to conserve the required function (induction of chondrocyte redifferentiation).*** Clearly, such does not constitute disclosure of a representative number of examples of, nor adequate written description for, the claimed genus.

Therefore, Applicants arguments are not persuasive.

With respect to the rejection of claims 58-62 and 74-77 under 35 US 112, 1st paragraph (scope of enablement), Applicants' arguments are persuasive and the enablement rejection of the claims is withdrawn.

With respect to the rejection of claims under 35 USC 102(e) and 35 USC 103(a), Applicant argue that the HOLTZMAN reference (U.S. Publication No. 2002/0055139 A1) is not prior art in view of the Declaration under 37 CFR 1.131 by Drs. Desnoyers et al. (submitted 10/5/2005). However, the Declaration filed on 10/5/2005 under 37 CFR 1.131 has not been considered because it is defective. Specifically, the Declaration is defective because it is not signed. Since the Declaration has not been considered, it is ineffective to overcome the HOLTZMAN reference (U.S. Pub. No. 2002/0055139 A1). Since the Declaration is ineffective to overcome the HOLTZMAN reference Applicants arguments are not persuasive and the rejection of the claims under 35 USC 102(e) and 35 USC 103(a) are maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J.E. Angell, Ph.D.
Art Unit 1635

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER